

Remarks

I. The Specification

A. Incorporation-by-Reference of the Sequence Listing

Applicants have amended the specification to contain an incorporation-by-reference of the material in the text file of the Sequence Listing in a separate paragraph identifying the name of the text file, the date of creation, and the size of the text file in bytes as per 37 C.F.R. § 1.52(e)(5).

B. Brief Description of the Drawings

The Brief Description of Figures 6 and 7, has been amended to refer to appropriate SEQ ID numbers. The SEQ ID numbers correspond to sequences shown in Figures 6 and 7. Therefore, no new matter is added by way of this amendment.

C. Claims

Upon entry of the foregoing amendment, claims 3-6 and 8-20 are pending in the application, with claim 3, 9, 11-15 and 20 being the independent claims. Claims 8, 16 and 17 are sought to be amended. Claim 7 is sought to be cancelled. No new matter is added by way of these amendments. It is respectfully requested that the amendments be entered and considered.

II. Computer Readable Form of the Sequence Listing

Applicants submit herewith a Computer Readable Form of the Sequence Listing in the form of a text file. The undersigned states that the Computer Readable Form of the Sequence Listing is submitted in accordance with 37 C.F.R. §§ 1.821 (c) and (e).

SEQ ID NOs:21-32 have been added to the Sequence Listing, submitted herewith. SEQ ID NOs:21-32 correspond to the sequences disclosed in Figures 6 and 7. Therefore, the Sequence Listing submitted herewith does not include any new matter which goes beyond the disclosure of the application as filed.

Applicants respectfully request the Commissioner to replace the Sequence Listing with the Sequence Listing, submitted herewith, and to include the Sequence Listing, submitted herewith, as part of the application.

III. Summary of Interview

Applicants gratefully acknowledge the courtesies extended by Examiner Mary E. Mosher, Ph.D., during a telephone interview on October 14, 2008, with Applicants' representative, Doug Golightly.

The objection of the disclosure with regards to Figures 6, 7 and 11-16 allegedly containing sequence recitations that are not accompanied by the required SEQ ID NOs was discussed. The Examiner and Applicants' representative discussed how to amend the specification and possibly the Sequence Listing to overcome the objection. The Examiner provided Applicants with several suggestions. Applicants' representative also noted that the descriptions of Figures 11-16 do refer to appropriate SEQ ID numbers. However, no definitive agreements were reached.

IV. Objection of the Specification

The Examiner objects to Figures 6, 7 and 11-16 as containing sequence recitations that are not accompanied by the required SEQ ID numbers. (Office Action, page 2.) The Examiner suggests amending the Brief Description of the Drawings. (Office Action, page 2.)

Applicants respectfully note that the Brief Description of the Drawings includes SEQ ID numbers for Figures 11-16. Therefore, Applicants believe that the objection is moot with regards to Figures 11-16.

Regarding Figures 6 and 7, Applicants have amended the specification herein to refer to the appropriate SEQ ID numbers. Also, as discussed herein, Applicants have submitted herewith a new Sequence Listing that includes sequences referred to in Figures 6 and 7.

In view of the above, Applicants respectfully request the Examiner reconsider and withdraw the objections of the specification.

V. Claim Rejections Under 35 U.S.C § 112

A. Claim 7

Solely to advance prosecution, and not in acquiescence to the Examiner's rejection, Applicants have herein cancelled claim 7, thereby rendering moot all of the rejections of claim 7 under 35 U.S.C. § 112.

B. Claim 8

The Examiner has rejected claim 8 under 35 U.S.C. § 112, second paragraph, as being indefinite as depending from a cancelled claim. (Office Action, page 3.) Applicants thank the Examiner for noting the error.

Applicants have amended claim 8 to depend from claim 3. Therefore, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claim 8 under 35 U.S.C. § 112, second paragraph.

VI. Claim 4 Is In Proper Dependent Form

The Examiner objects to claim 4 "under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim Claim 4 is drawn to a Markush group of mutations which includes species (e.g. V221F) which are outside the scope of parent claim 3." (Office Action, page 4.) Applicants respectfully disagree.

Claim 3 refers to a mutant VSV having the mutation $\Delta M51$ in the gene encoding the M protein. Claim 4 further limits claim 3 by requiring an additional mutation(s) selected from those in the Markush group. Since claim 4 requires at least one mutation in addition to the mutation $\Delta M51$, claim 4 does further limit the subject matter of claim 3.

In view of the above, Applicants respectfully request the Examiner to reconsider and withdraw the objection of claim 4 under 37 C.F.R. § 1.75(c).

VII. The Claimed Invention is Not Obvious

A. Claims 3-5, 9-15 and 20

“Claims 3-5, 9-15 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitt et al US2005/0260601.” (Office Action, page 5.) Applicants respectfully disagree.

As a preliminary matter, Applicants point out that the present application claims priority to US Provisional Application No. 60/457,591 filed March 27, 2003 and this provisional application provides full support for the pending claims of the present application. For example, see page 14, lines 14-18; page 15, lines 6-17; Figures 6 & 7; and claims 4-20 of US Provisional Application No. 60/457,591.

Whitt *et al.* was filed September 8, 2003 which is after the March 27, 2003 filing date of Applicants’ US Provisional Application No. 60/457,591 to which the present application claims priority. Therefore, the disclosure of Whitt *et al.* US2005/0260601 is not available as prior art to the present application.

The provisional application to which Whitt *et al.* US2005/0260601 claims priority (60/408,908) was filed on September 9, 2002. Applicants note that the disclosure of the ‘908 application is significantly different than that of Whitt *et al.* US2005/0260601. Therefore, Applicants address the rejection of claims 3-5, 9-15 and 20 under 35 U.S.C. § 103(a) with regards only to US Provisional Application No. 60/408,908 (the ‘908 application).¹

i. No Expectation of Success

The Examiner states,

Whitt differs from the claimed invention in that Whitt does not specifically teach deletion of the M51 residue. However, Whitt broadly teaches mutation or partial deletion of the M protein . . . and teaches substitution mutation of residues 51 and 226. It would have been within the ordinary skill of the art to make a partial deletion that removed residue 51, for the purpose of creating a more reversion-resistant virus, and to incorporate multiple mutations for the same purpose. Therefore the invention as a whole is *prima facie* obvious, absent unexpected results.

(Office Action, pages 5-6.) Applicants respectfully disagree.

¹ Applicants do not concede that US Provisional Application No. 60/408,908 is prior art and reserve the right to prove that this provisional application is not prior art to the present application.

The Examiner must show that there is a reasonable expectation of success in combining the references. (*In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991).) The Examiner has not addressed this issue.

In the outstanding Office Action, the Examiner has cited Lichty *et al.* ((2006) Journal of Virology 87:3379-3384) and pointed to the last paragraph which describes the inability of the authors to obtain VSV viruses bearing particular mutations. This illustrates how one skilled in the art, at the time of the invention, would not have had a reasonable expectation that they could obtain a VSV containing a deletion of M51 in the M protein. Lichty *et al.* is not prior art to the present application, but if there was no reasonable expectation even in 2006, then *a fortiori* there would not have been a reasonable expectation at the effective filing date(s) of the present application.

The '908 application does discuss a substitution at M51, but never discloses or suggests a specific deletion of M51. Additionally, the '908 application does not show working examples of any virus with any deletion in the M protein. The Examiner alleges that one skilled in the art would delete M51 "for the purpose of creating a more reversion-resistant virus". (Office Action, pages 5-6.) However, this logic does not follow, since the '908 application discusses the importance of a M51A substitution and even has claims related to this substitution, but never discloses or suggests a particular deletion of M51.

In summary, until the disclosure of Applicants' invention, one skilled in the art would not have had a reasonable expectation of success of obtaining a VSV with the Δ M51 mutation in the M protein.

ii. Unexpected Results

The Manual Of Patent Examining Procedure (MPEP; E8r7) states,

[e]vidence of unobvious or unexpected advantageous properties, such as superiority in a property the claimed compound shares with the prior art, can rebut *prima facie* obviousness. 'Evidence that a compound is unexpectedly superior in one of a spectrum of common properties . . . can be enough to rebut a *prima facie* case of obviousness.' No set number of examples of superiority is required. *In re Chupp*, 816 F.2d 643, 646, 2 USPQ2d 1437, 1439 (Fed. Cir. 1987)

(MPEP, 716.02(a)II.)

The Examiner states, "the invention as a whole is *prima facie* obvious, absent unexpected results." (Office Action, page 6, underlining added.)

The '908 application consistently describes how viruses with mutant M proteins are non-cytopathic, *e.g.*, see page 1, lines 7-11; page 3, line 19-21; page 5, line 24-25; page 12, line 3; Figure 1; and ALL of the claims. Therefore, one skilled in the art upon review of the '908 application would have expected a VSV with a Δ M51 mutation of the M protein to be non-cytopathic. On the contrary, Applicants' specification demonstrates oncolytic and cytopathic properties of a VSV with the Δ M51 mutation. One skilled in the art at the time of the invention, *e.g.*, based on the disclosure of the '908 application, would have been surprised that a VSV with the Δ M51 mutation would demonstrate oncolytic and/or cytopathic properties.

In view of the above, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 3-5, 9-15 and 20 under 35 U.S.C. § 103(a).

B. Claims 4-6 and 8

"Claims 4-6, 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitt *et al* US2005/0260601 as applied to claim 3 above, and further in view of Desforges *et al* (Virus Research 76:87-102, 2001, cited in IDS)." (Office Action, page 6.) Applicants respectfully disagree.

Whitt *et al.* and the '908 application are discussed above. Desforges *et al.* does not cure the deficiencies of the '908 application.

Applicants respectfully request the Examiner to reconsider and withdraw the rejection of claims 4-6 and 8 under 35 U.S.C. § 103(a).

Conclusion

It is not believed that extensions of time are required beyond those that may otherwise be provided for herein or in accompanying documents. However, if additional extensions of time are necessary to prevent abandonment of this application, The United States Patent and Trademark Office is hereby authorized to charge any fee deficiency required to prevent abandonment of the current application or credit any overpayment to Deposit Account 50-1677.

Applicants believe that a full and complete Reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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